

Date of Deposit November 2, 2001

Printed Name Olga M Frontz

Oliver M. French
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Charles Jack Fisher et al.
For : METHODS FOR TREATING SEPSIS
Docket No. : X-12444A

Assistant Commissioner for Patents
Washington, D. C. 20231
Sir:

Please amend the accompanying application as

Please insert the following new first paragraph:

This case is a continuation of U.S. Serial No. 09/425,181 filed October 22, 1999, which claims the benefit of provisional application 60/105,239 filed October 22, 1998.

Please add the following new claims 16-32 and cancel Claims 1-15.

--16. A method of treating a human patient with sepsis which comprises, administering a continuous infusion of

Figure 1 consists of 12 line graphs arranged in a 3x4 grid. Each graph plots 'Plasma concentration (mg/ml)' on the y-axis (0 to 1.0) against 'Time (h)' on the x-axis (0 to 12). The four groups are: (a) control, (b) 100 mg/kg diazepam, (c) 100 mg/kg diazepam + 100 mg/kg diazepam, and (d) 100 mg/kg diazepam + 100 mg/kg diazepam. All groups show a peak concentration around 2-4 hours. Group (d) shows the highest peak concentration, followed by (c), (b), and (a).

5.0 $\mu\text{g/kg/hr}$ to 30 $\mu\text{g/kg/hr}$ of recombinant human activated protein C in combination with bacterial/permeability increasing (BPI) protein.

17. The method of Claim 16 wherein the BPI protein is recombinantly produced and is administered as a continuous infusion at about 50 $\mu\text{g/kg/hr}$ to about 300 $\mu\text{g/kg/hr}$.

18. The method of Claim 16 wherein the BPI protein is recombinantly produced and is administered as a continuous infusion at about 100 $\mu\text{g/kg/hr}$ to about 200 $\mu\text{g/kg/hr}$.

19. The method of any one of claims 16, 17, or 18 wherein the protein C plasma ranges in the human patient are from about 30 ng/ml to about 150 ng/ml.

20. The method of Claim 19 wherein the protein C plasma range in the human patient is 100 ng/ml.

21. The method of Claim 16 wherein about 0.1 mg/kg to about 10 mg/kg intravenous bolus of the BPI protein is administered followed by a continuous infusion of the BPI protein.

22. The method of Claim 19 wherein about 0.1 mg/kg to about 10 mg/kg intravenous bolus of BPI protein is administered followed by the continuous infusion.

23. The method of Claim 16 wherein the BPI protein is administered as an intermittent injection.

24. The method of Claim 16 wherein the human activated protein C infusion is administered for about 1 hour to about 240 hours.

25. The method of Claim 19 wherein the human activated protein C infusion is administered for about 1 hour to about 240 hours.

26. The method of Claim 17 wherein the BPI protein is administered for about 48 hours.

27. The method of Claim 18 wherein the BPI protein is administered for about 48 hours.

28. The method of Claim 24 wherein the BPI protein is administered for about 48 hours.

29. The method of Claim 17 wherein the BPI protein is administered for 24 to 240 hours.

30. The method of Claim 18 wherein the BPI protein is administered for 24 to 240 hours.

31. The method of Claim 24 wherein the BPI protein is administered for 24 to 240 hours.

32. The method of any one of Claim 26, 27, 28, 29, 30 or 31 wherein the human activated protein C infusion and the BPI infusion are administered simultaneously.--

Remarks

This case is a continuation of U.S. Serial No. 09/425,181 filed October 22, 1999 (allowed). The Specification has been amended to update the priority information. New claims 16-32 are also being added via this amendment. Support for the claims may be found throughout the Specification, for example: Claim 16 (page 8, lines 21 and 22); Claims 17 and 18 (page 11, lines 5-8); Claims 19 and 20 (page 8, lines 33 and 34); Claims 21-23 (page 11, lines 8-14); Claims 24 and 25 (page 8, lines 8-11); Claims 26-28 (page 18, lines 2-4); Claims 29-31 (page 11, lines 8-12) and Claims 32 (page 10, lines 22-24 and page 18, lines 4-6). No new matter has been added by this amendment. Entry of the amendment is requested.

Applicants assert that the application is in condition for allowance and request that you contact the undersigned with any questions.

Respectfully submitted,

Brian P. Barrett

Brian P. Barrett
Attorney for Applicants
Registration No. 39,597
Phone: 317-276-7243

Eli Lilly and Company
Patent Division/BPB
Lilly Corporate Center
Indianapolis, Indiana 46285

November 1, 2001

0959333-10203
FO2001-6585550

[illegible]

New Claims after Preliminary Amendment

24. The method of Claim 16 wherein the human activated protein C infusion is administered for about 1 hour to about 240 hours.

25. The method of Claim 19 wherein the human activated protein C infusion is administered for about 1 hour to about 240 hours.

26. The method of Claim 17 wherein the BPI protein is administered for about 48 hours.

27. The method of Claim 18 wherein the BPI protein is administered for about 48 hours.

28. The method of Claim 24 wherein the BPI protein is administered for about 48 hours.

29. The method of Claim 17 wherein the BPI protein is administered for 24 to 240 hours.

30. The method of Claim 18 wherein the BPI protein is administered for 24 to 240 hours.

31. The method of Claim 24 wherein the BPI protein is administered for 24 to 240 hours.

32. The method of any one of Claim 26, 27, 28, 29, 30 or 31 wherein the human activated protein C infusion and the BPI infusion are administered simultaneously.

099999-11001
102011-102011